PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P208356PCT FC	OR FURTHER ACTION	See Form PCT/PEA/16
	emetional filing date (day/month/year)	Priority date (day/month/year) 24.10.2003
International Patent Classification (IPC) or national A23L1/29, A23L1/30, A61K31/733, A61K	I classification and IPC 31/702, A61K35/74, A61P37/00	
Applicani N.V. NUTRICIA et al.		
The state of the partie of the state of the	ract to me abbitcaut accomitte to VIIIC	y this International Prefiminary Examining le 36.
2. This REPORT consists of a total of 5 e	heets, including this cover sheet	
3. This report is also accompanied by ANI		
a. 🗵 sent to the applicant and to the l	international Bureau) a total of 3 she	eets, as follows:
Administrative Instructions).	tames to the entire term by this Authoriti	en amended and are the basis of this report y (see Rule 70.16 and Section 607 of the
 sheets which supersede ear beyond the disclosure in the Supplemental Box, 	fler sheels, but which this Authority of international application as lited, as i	onsiders contain an amendment that goes indicated in item 4 of Box No. I and the
	only) a total of (Indicate type and nur lated thereto, in compuler readable fo g (see Section 802 of the Administrati	mber of electronic carrier(s)) , containing a prim only, as indicated in the Supplemental ive instructions).
4. This report contains indications relating	to the following liams:	
_	to the londering items.	
Box No. I Basks of the opinion Box No. II Priority		
	Onlain with regard to accuse the con-	
Box No. IV Lack of unity of inventi	opinion with regard to novelty, inventi	ive step and industrial applicability
Box No. V Reasoned statement usapplicability; citations applicability; citations applicability.	Inder Article 35(2) with regard to nove and explanations supporting such stat	elly, inventive step or industrial
Box No. VI Certain documents cite	ed	
Box No. Vil Certain defects in the in	nternational application	
⊠ Box No. VIII Certain observations of	n the international application	
Date of submission of the demand	Date of completion of	this report
23.08.2005	15.12,2005	
Hame and mailing address of the international internationa	Authorized Officer	
European Palem Office 0.80298 Munich Tel. +49 89 2398 • 0 Tx: 523656 epmu	Barnas, C	
Fax: +49 89 2399 - 4465	Telephone No. +49 89	2399-7469

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/NL2004/000748

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_	Box No. Basis of the repo	
1	. With regard to the language, the filed, unless otherwise indicates	nls report is based on the international application in the language in which it was
	many in this loanguage of a	nslations from the original language into the following language , translation lurnished for the purposes of:
	 ☐ international search (un ☐ publication of the intern ☐ international preliminary 	der Rules 12.3 and 23.1(b)) attonal application (under Rule 12.4) rexamination (under Rules 55.2 and/or 55.3)
2.	. With regard to the elements' on have been furnished to the receive report as "originally filed" and as	the international application, this report is based on (replacement sheets which iving Office in response to an invitation under Article 14 are referred to in this report):
	Description, Pages	
	1-34	es published
	Sequence listings part of the des	cription, Pages
	1-8	received on 03,01.2005 with letter of 03.01.2005
	Claims, Numbers	
	1-18	received on 23.08.2005 with latter of 22,08.2005
	Drawings, Sheets	
	1, 2	benzilduq aa
	⊠ a sequence listing and/or any	related table(s) - see Supplemental Box Relating to Sequence Listing
3.	The amendments have result	
	the description, pagesthe claims, Nos.	: · ·
	the drawings, sheets/ligs the sequence listing (spec	
	any table(s) related to sec	uence listing (specify);
4. [}	This report has been establis nad not been made, since they has Supplemental Box (Rule 70.2(c)).	hed as if (some of) the amendments annexed to this report and listed below we been considered to go beyond the disclosure as filed, as indicated in the
Ì	The description, pages	The state of the s
	the claims, Nos. the drawings, sheets/figs	
	U the sequence listing (spec	ify):
	any table(s) related to seq	•••
•	Lr lem 4 applies, som	e or all of these sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/NL2004/000748

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims

No:

1-18

Inventive step (IS)

Yes: Claims

Claims

1-18

No: Claims

Industrial applicability (IA)

Yes: Claims

1-18

No: Claims

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/NL2004/000748

Sup	plemental Box relating to Sequence Listing
Contin	lation of Box I, Item 2:
1. With nece	regard to any nucleotide and/or amino acid sequence disclosed in the international application and essary to the claimed invention, this report has been established on the basis of:
a. ty	pe of materials
8	a sequence listing
Ø	table(s) related to the sequence listing
b. for	mat of material;
⊠	in written format
Ø	in computer readable form
c. tim	e of filing/furnishing:
	contained in the international application as filed
	filed together with the international application in computer readable form
Ø	furnished subsequently to this Authority for the purposes of search and/or examination
Ø	received by this Authority as an amendment on
a	a addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating stere has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as file

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No.

PCT/NL2004/000748

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The documents mentioned in the present International Preliminary Report are numbered as in the International Search Report. D1 corresponds to the first document of the Search Report, D2 to the second document etc.

Art. 33(3) PCT

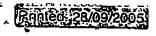
D2 discloses mixtures of at least two non-digestible soluble carbohydrate components having a different structure and differing in the average length by at least 5 monosaccharides. The problem to be solved is the provision of a carbohydrate mixture for improving the intestinal flora. The problem is solved by providing a preparation as described in claim 1 which, in addition, comprises Bifidobacterium breve. The cited prior an does not contain any hint that would prompt the skilled person to provide such a preparation. Claims 1-17 are therefore inventive. The cited prior art does also not contain any hint that would prompt the skilled person to use a mixture as described in claim 18 for the manufacture of a composition for decreasing the relative amounts of the indicated bacteria. Said claim is therefore also inventive.

Re Item VIII

Certain observations on the international application

Art. 6 PCT

The wording of claim 4 ("... wherein the carbohydrate components comprises 95 to 60 wt% and the carbohydrate B comprises 5 to 40 wt% with A + B = 100%.") cannot be understood from the technical point of view. Said claim is therefore not clear, contrary to Art. 6 PCT. In view of the description of the present application said claim has been examined as "... wherein the carbohydrate component A comprises 95 to 60 wt% and the carbohydrate B comprises 5 to 40 wt% with A + B = 100%."



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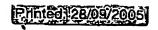
Amended claims



1. A preparation comprising Bifldobacterium breve and a mixture of at least two non-digestible soluble carbohydrate components A and B, wherein

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- said carbohydrate component A has a different structure from said carbohydrate component B;
- said carbohydrate component A is present in an amount of 5 to 95 % by weight of the sum of carbohydrate components A and B;
- at least 50% of the total non-digestible soluble carbohydrates is selected from disaccharides to eicosasaccharides; and
- carbohydrate components A and B differ in the (average) number of monosaccharide units, carbohydrate component A having an average chain length which is at least 5 monosaccharide units lower than the average chain length of component B.
- 2. A preparation according to claim 1, wherein said carbohydrate components A and B differ in the structure of the monosaccharide units of the carbohydrate.
- 3. A preparation according to claim 1 or 2, wherein said carbohydrate component A is selected from indigestible monosaccharides up to hexasaccharides of the same carbohydrate structure, and said carbohydrate component B is selected from indigestible heptasaccharides and higher polysaccharides of the same carbohydrate structure.
- A preparation according to any one of claims 1-3, wherein the carbohydrate
 components comprises 95 to 60 wt% and the carbohydrate B comprises 5 to 40 wt%, with A + B = 100 wt%.
- A preparation according to any one of claims 1-4, wherein at least 60 wt%, preferably 80 to 100 wt% of said carbohydrate component A belong to the group of galacto-oligosaccharides, preferably to the group of trans-galacto-oligosaccharides.



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- 6. A preparation according to any one of claims 1-5, wherein at least 60 wt%, preferably 80 to 100 wt% of said carbohydrate component B belong to the group of fructo-polysaccharides, including inulin.
- 5 7. A preparation according to any one of claims 1-6, comprising 10⁵ to 10¹¹ cfu of Bifidobacterium breve per g of total non-digestible soluble carbohydrate.
 - 8. A preparation according to any one of claims 1-7 for use as a supplement, wherein the probiotic *Bifldobacterium breve* is present in the supplement in an amount of 1x10⁵ to 1.5x10¹¹ cfu/g, calculated on the basis of the supplement.
 - 9. A preparation according to any one of claims 1-7 for use as an infant nutrition, wherein the Bifidobacterium breve is present in the supplement in an amount of 1×10^2 to 1×10^{12} cfu/g of the infant supplement.

10. An infant nutrition supplement comprising a preparation according to any one of claims 1-8, and further comprising digestible carbohydrate, a lipid source, or a protein source, or a mixture thereof.

- 20 11. An infant nutrition comprising a preparation according to any one of claims 1-7 and 9, and further comprising digestible carbohydrate, a lipid source, and a protein source.
- 12. Use of a preparation according to any one of claims 1-9 for the manufacture of a composition for the normalisation of the Bifidobacterium species composition in the gastro-intestinal tract of non- or partially breast-fed infants to the composition in breast-fed infants.
- 13. Use of a preparation according to any one of claims 1-9 for the manufacture of a
 composition for the prevention or treatment of one or more immune disorders.



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- 14. Use according to claim 13, wherein said immune disorders are selected from allergy, atopy, allergic rhinitis, food hypersensitivity, atopic dermatitis, eczema and asthma.
- 5 15. Use according to claim 13 or 14, wherein said immune disorders are selected from diarrhoea and viral diarrhoea.
 - 16. Use of a preparation according to any one of claims 1-9 for the manufacture of a composition for preventing and/or treating energy malabsorption.
 - 17. Use of a preparation according to any one of claims 1-9 for the manufacture of a composition for inhibiting the infiltration of eosinophils, neutrophils and mononuclear cells in allergic lesions, inhibiting the Th2 type immune response and/or stimulating the Th1 mediated immune response.
 - 18. Use of a mixture of at least two non-digestible soluble carbohydrate components A and B, wherein
 - said carbohydrate component A is present in an amount of from 5 to 95 % by weight of the sum of carbohydrate components A and B;
- at least 50% of the total πon-digestible soluble carbohydrates is selected from disaccharides to eicosasaccharides; and
 - said carbohydrate components A and B differ (i) in the (average) number of monosaccharide units of the carbohydrate, (ii) in the structure of the monosaccharide units of the carbohydrate, or (iii) both,
- 25 for the manufacture of a composition for decreasing the relative amounts of Bifidobacterium catenulatum, B. pseudocatenulatum and/or B. adolescentis in the gastro-intestinal tract of non- or partially breast-fed infants.





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